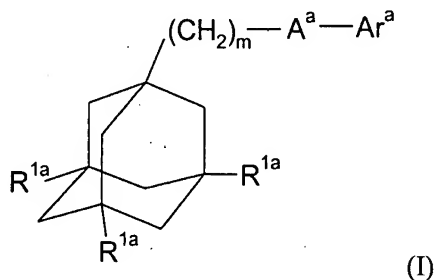


Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

1. (Currently amended) A method of treating a patient comprising administering simultaneously, sequentially, or separately a therapeutically effective amount of a pharmaceutical product comprising, in combination, a preparation of a first active ingredient which is a P2X₇ receptor antagonist which P2X₇ receptor antagonist is an adamantyl derivative, and a preparation of a second active ingredient which is a tumour necrosis factor α (TNF α) inhibitor, ~~for simultaneous, sequential or separate use in therapy.~~
2. (Currently amended) ~~A composition~~ The method according to claim 1 wherein the P2X₇ receptor antagonist is a compound of formula

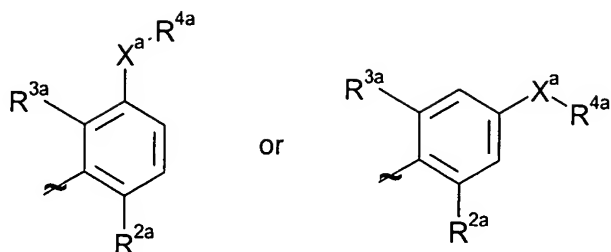


wherein m represents 1, 2 or 3;

each R^{1a} independently represents a hydrogen or halogen atom;

A^a represents C(O)NH or NHC(O);

Ar^a represents a group



X^a represents a bond, an oxygen atom or a group CO, $(CH_2)_{1-6}$, $CH=$, $(CH_2)_{1-6}O$, $O(CH_2)_{1-6}$, $O(CH_2)_{2-6}O$, $O(CH_2)_{2-3}O(CH_2)_{1-3}$, $CR'(OH)$, $(CH_2)_{1-3}O(CH_2)_{1-3}$, $(CH_2)_{1-3}O(CH_2)_{2-3}O$, NR^{5a} , $(CH_2)_{1-6}NR^{5a}$, $NR^{5a}(CH_2)_{1-6}$, $(CH_2)_{1-3}NR^{5a}(CH_2)_{1-3}$, $O(CH_2)_{2-6}NR^{5a}$, $O(CH_2)_{2-3}NR^{5a}(CH_2)_{1-3}$, $(CH_2)_{1-3}NR^{5a}(CH_2)_{2-3}O$, $NR^{5a}(CH_2)_{2-6}O$, $NR^{5a}(CH_2)_{2-3}O(CH_2)_{1-3}$, $CONR^{5a}$, $NR^{5a}CO$, $S(O)_n$, $S(O)_nCH_2$, $CH_2S(O)_n$, SO_2NR^{5a} or $NR^{5a}SO_2$;

n is 0, 1 or 2;

R' represents a hydrogen atom or a C_1 - C_6 alkyl group;

one of R^{2a} and R^{3a} represents a halogen, cyano, nitro, amino, hydroxyl, or a group selected from (i) C_1 - C_6 alkyl optionally substituted by at least one C_3 - C_6 cycloalkyl, (ii) C_3 - C_8 cycloalkyl, (iii) C_1 - C_6 alkyloxy optionally substituted by at least one C_3 - C_6 cycloalkyl, and (iv) C_3 - C_8 cycloalkyloxy, each of these groups being optionally substituted by one or more fluorine atoms, and the other of R^{2a} and R^{3a} represents a hydrogen or halogen atom;

either R^{4a} represents a 3- to 9-membered saturated or unsaturated aliphatic heterocyclic ring system containing one or two nitrogen atoms and optionally an oxygen atom, the heterocyclic ring system being optionally substituted by one or more substituents independently selected from fluorine atoms, hydroxyl, carboxyl, cyano, C_1 - C_6 alkyl, C_1 - C_6 hydroxyalkyl, $-NR^{6a}R^{7a}$, $-(CH_2)_rNR^{6a}R^{7a}$ and $-CONR^{6a}R^{7a}$,

or R^{4a} represents a 3- to 8-membered saturated carbocyclic ring system substituted by one or more substituents independently selected from $-NR^{6a}R^{7a}$, $-(CH_2)_rNR^{6a}R^{7a}$ and $-CONR^{6a}R^{7a}$, the ring system being optionally further substituted by one or more substituents independently selected from fluorine atoms, hydroxyl and C_1 - C_6 alkyl;

r is 1, 2, 3, 4, 5 or 6;

R^{5a} represents a hydrogen atom or a C_1 - C_6 alkyl or C_3 - C_8 cycloalkyl group;

R^{6a} and R^{7a} each independently represent a hydrogen atom or a C_1 - C_6 alkyl, C_2 - C_6 hydroxyalkyl or C_3 - C_8 cycloalkyl group, or R^{6a} and R^{7a} together with the nitrogen atom to which they are attached form a 3- to 8-membered saturated heterocyclic ring;

with the provisos that,

(a) when A^a represents $C(O)NH$ and R^{4a} represents an unsubstituted 3- to 8-membered saturated aliphatic heterocyclic ring system containing one nitrogen atom, then X^a is other than a bond, and

(b) when A^a represents $C(O)NH$ and X^a represents a group $(CH_2)_{1-6}$ or $O(CH_2)_{1-6}$, then R^{4a} does not represent an unsubstituted imidazolyl, unsubstituted morpholinyl, unsubstituted piperidinyl or unsubstituted pyrrolidinyl group, and

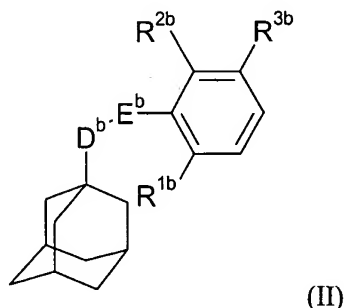
(c) when A^a represents $NHC(O)$ and R^{4a} represents an unsubstituted 3- to 8-membered saturated aliphatic heterocyclic ring system containing one nitrogen atom, then X^a is other than a bond, and

(d) when A^a represents $NHC(O)$ and X^a represents $O(CH_2)_{1-6}$, $NH(CH_2)_{1-6}$ or SCH_2 , then R^{4a} does not represent an unsubstituted 1-piperidinyl or unsubstituted 1-pyrrolidinyl group, and

(e) when A^a represents $NHC(O)$ and X^a represents $O(CH_2)_{2-3}NH(CH_2)_2$, then R^{4a} does not represent an imidazolyl group;

or a pharmaceutically acceptable salt or solvate thereof.

3. (Currently amended) ~~A composition~~ The method according to claim 1 wherein the $P2X_7$ receptor antagonist is a compound of formula

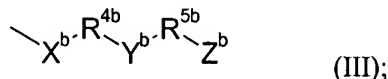


wherein D^b represents CH₂ or CH₂CH₂;

E^b represents C(O)NH or NHC(O);

R^{1b} and R^{2b} each independently represent a hydrogen or halogen atom, or an amino, nitro, C₁-C₆ alkyl or trifluoromethyl group;

R^{3b} represents a group of formula



X^b represents an oxygen or sulphur atom or a group NH, SO or SO₂;

Y^b represents an oxygen or sulphur atom or a group NR^{11b}, SO or SO₂;

Z^b represents a group -OH, -SH, -CO₂H, C₁-C₆ alkoxy, C₁-C₆ alkylthio,

C₁-C₆-alkylsulphinyl, C₁-C₆-alkylsulphonyl, -NR^{6b}R^{7b}, -C(O)NR^{8b}R^{9b}, imidazolyl,

1-methylimidazolyl, -N(R^{10b})C(O)-C₁-C₆ alkyl, C₁-C₆ alkylcarbonyloxy,

C₁-C₆ alkoxycarbonyloxy, -OC(O)NR^{12b}R^{13b}, -OCH₂OC(O)R^{14b}, -OCH₂OC(O)OR^{15b} or -OC(O)OCH₂OR^{16b};

R^{4b} represents a C₂-C₆ alkyl group;

R^{5b} represents a C₁-C₆ alkyl group;

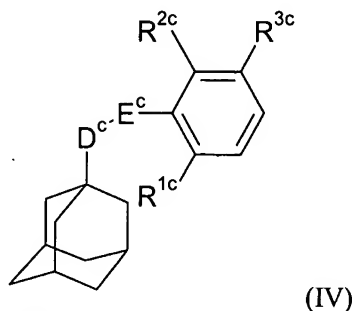
R^{6b}, R^{7b}, R^{8b}, R^{9b}, R^{10b}, R^{12b} and R^{13b} each independently represent a hydrogen atom, or a C₁-C₆ alkyl group optionally substituted by at least one hydroxyl group;

R^{11b} represents a hydrogen atom, or a C₁-C₆ alkyl group optionally substituted by at least one substituent independently selected from hydroxyl and C₁-C₆ alkoxy; and

R^{14b}, R^{15b} and R^{16b} each independently represent a C₁-C₆ alkyl group;

with the provisos that (i) when E^b represents NHC(O), X^b represents O, S or NH and Y^b represents O, then Z^b represents -NR^{6b}R^{7b} where R^{6b} represents a hydrogen atom and R^{7b} represents either a hydrogen atom or a C₁-C₆ alkyl group substituted by at least one hydroxyl group, and (ii) when E^b represents NHC(O), X^b represents O, S or NH, Y represents NH and R^{5b} represents CH₂CH₂, then Z^b is not -OH or imidazolyl; or a pharmaceutically acceptable salt or solvate thereof.

4. (Currently amended) ~~A composition~~ The method according to claim 1 wherein the P2X₇ receptor antagonist is a compound of formula

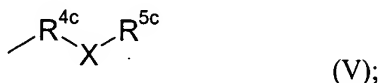


wherein D^c represents CH₂ or CH₂CH₂;

E^c represents C(O)NH or NHC(O);

R^{1c} and R^{2c} each independently represent hydrogen, halogen, amino, nitro, C₁-C₆ alkyl or trifluoromethyl, but R^{1c} and R^{2c} may not both simultaneously represent hydrogen;

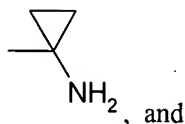
R^{3c} represents a group of formula



R^{4c} represents a C₁-C₆ alkyl group;

X^c represents an oxygen or sulphur atom or a group NR^{13c}, SO or SO₂;

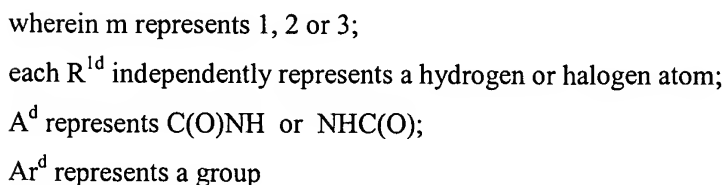
R^{5c} represents hydrogen, or R^{5c} represents C₁-C₆ alkyl or C₂-C₆ alkenyl, each of which may be optionally substituted by at least one substituent selected from halogen, hydroxyl, (di)-C₁-C₆-alkylamino, -Y^c-R^{6c},

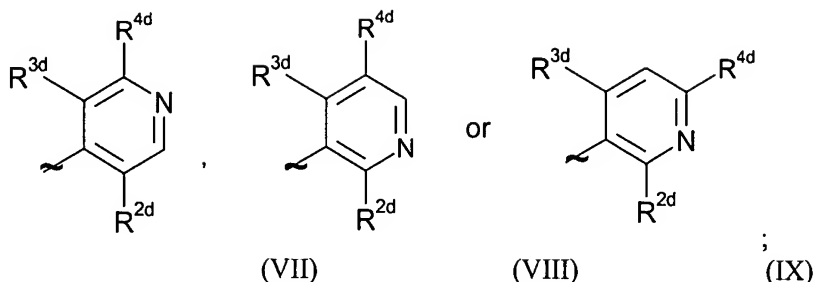


a 5- or 6-membered heteroaromatic ring comprising from 1 to 4 heteroatoms independently selected from nitrogen, oxygen and sulphur which heteroaromatic ring may itself be optionally substituted by at least one substituent selected from halogen, hydroxyl and C₁-C₆ alkyl;

Y^c represents an oxygen or sulphur atom or a group NH, SO or SO₂;

5. (Currently amended) ~~A composition~~ The method according to claim 1 wherein the P2X₇ receptor antagonist is a compound of formula





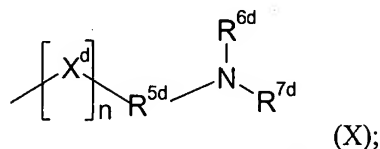
one of R^{2d} and R^{3d} represents halogen, nitro, amino, hydroxyl, or a group

selected from (i) C₁-C₆ alkyl optionally substituted by at least one halogen atom,

(ii) C₃-C₈ cycloalkyl, (iii) C₁-C₆ alkoxy optionally substituted by at least one halogen atom, and

(iv) C₃-C₈ cycloalkyloxy, and the other of R^{2d} and R^{3d} represents a hydrogen or halogen atom;

R^{4d} represents a group



X^d represents an oxygen or sulphur atom or a group >N-R^{8d};

n is 0 or 1;

R^{5d} represents a C₁-C₅ alkyl group which may be optionally substituted by at least one substituent selected from hydroxyl, halogen and C₁-C₆ alkoxy;

R^{6d} and R^{7d} each independently represent a hydrogen atom, C₁-C₆ alkyl (optionally substituted by at least one substituent selected from hydroxyl, halogen, C₁-C₆ alkoxy, and (di)-C₁-C₄ alkylamino (itself optionally substituted by at least one hydroxyl group)), or C₃-C₈ cycloalkyl (optionally substituted by at least one substituent selected from hydroxyl, halogen and C₁-C₆ alkoxy); and

R^{8d} represents a hydrogen atom or a C₁-C₅ alkyl group which may be optionally substituted by at least one substituent selected from hydroxyl, halogen and C₁-C₆ alkoxy;

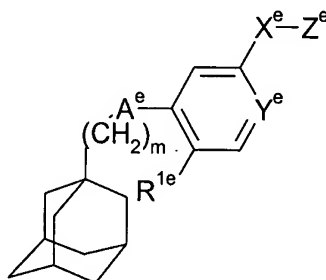
with the provisos that:

when n is 0, then A^d is NHC(O), and

when n is 1, X^d represents oxygen and A^d is C(O)NH, then R^{6d} and R^{7d} do not both simultaneously represent a hydrogen atom or do not both simultaneously represent an

unsubstituted C₁-C₆ alkyl, or when one of R^{6d} and R^{7d} represents a hydrogen atom, then the other of R^{6d} and R^{7d} does not represent an unsubstituted C₁-C₆ alkyl; and
when n is 1, X^d is oxygen, sulphur or >NH and A^d is NHC(O), then R^{6d} and R^{7d} do not both simultaneously represent a hydrogen atom or do not both simultaneously represent an unsubstituted C₁-C₆ alkyl, or when one of R^{6d} and R^{7d} represents a hydrogen atom, then the other of R^{6d} and R^{7d} does not represent an unsubstituted C₁-C₆ alkyl or -CH₂CH₂OH;
or a pharmaceutically acceptable salt or solvate thereof.

6. (Currently amended) ~~A composition~~ The method according to claim 1 wherein the P2X₇ receptor antagonist is a compound of formula



(XI)

wherein m represents 1, 2 or 3;

A^e represents C(O)NH or NHC(O);

Y^e represents N or CH;

X^e represents a bond, CO, (CH₂)₁₋₆, O(CH₂)₁₋₆, (CH₂)₁₋₆NH(CH₂)₁₋₆, (CH₂)₁₋₆O(CH₂)₁₋₆, NH(CH₂)₁₋₆;

Z^e represents NR^{2e}R^{3e};

R^{1e} represents halogen, cyano, nitro, amino, hydroxyl, C₁-C₆ alkyl or C₃-C₈ cycloalkyl, which alkyl or cycloalkyl group can be optionally substituted by one or more fluorine atoms;

R^{2e} and R^{3e} each independently represent a hydrogen atom, C₁-C₆ alkyl or C₃-C₈ cycloalkyl, which alkyl or cycloalkyl group can be optionally substituted by one or more groups selected from hydroxyl, halogen or C₁-C₆ alkoxy, or R^{2e} and R^{3e} together with the nitrogen atom to which they are attached form a 3- to 9-membered saturated mono- or bicyclic heterocyclic ring comprising from 1 to 2 nitrogen atoms and optionally an oxygen atom, which heterocyclic ring can be optionally substituted by one or more groups selected from hydroxyl, halogen or C₁-C₆ alkoxy; or a pharmaceutically acceptable salt or solvate thereof.

7. (Currently amended) ~~A composition~~ The method according to claim 1 wherein the P2X₇ receptor antagonist is:

2-Chloro-5-[[2-(2-hydroxy-ethylamino)-ethylamino]-methyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,

2-Chloro-5-[3-[(3-hydroxypropyl)amino]propyl]-N-(tricyclo[3.3.1.1]dec-1-ylmethyl)-benzamide,

(R)-2-Chloro-5-[3-[(2-hydroxy-1-methylethyl)amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,

2-Chloro-5-[[2-[(2-hydroxyethyl)amino]ethoxy]methyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,

2-Chloro-5-[3-[3-(methylamino)propoxy]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)benzamide,

2-Chloro-5-[3-(3-hydroxy-propylamino)-propoxy]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,

2-Chloro-5-[2-(3-hydroxypropylamino)ethylamino]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,

2-Chloro-5-[2-(3-hydroxypropylsulfonyl)ethoxy]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,

2-Chloro-5-[2-[2-[(2-hydroxyethyl)amino]ethoxy]ethoxy]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
2-Chloro-5-[[2-[(1-methyl-1*H*-imidazol-4-yl)ethyl]amino]ethyl]amino]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
2-Chloro-5-piperazin-1-ylmethyl-*N*-(tricyclo[3.3.1.1]dec-1-ylmethyl)-benzamide,
2-Chloro-5-(4-piperidinyloxy)-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
2-Chloro-5-(2,5-diazabicyclo[2.2.1]hept-2-ylmethyl)-*N*-(tricyclo[3.3.1.1]dec-1-ylmethyl)-benzamide,
2-Chloro-5-(piperidin-4-ylsulfinyl)-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
5-Chloro-2-[3-[(3-hydroxypropyl)amino]propyl]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-4-pyridinecarboxamide,
2-Chloro-5-[3-[[(1*R*)-2-hydroxy-1-methylethyl]amino]propyl]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-3-pyridinecarboxamide,
5-Chloro-2-[3-(ethylamino)propyl]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-4-pyridinecarboxamide,
5-Chloro-2-[3-[(2-hydroxyethyl)amino]propyl]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-4-pyridinecarboxamide,
5-Chloro-2-[3-[[(2*S*)-2-hydroxypropyl]amino]propyl]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-4-pyridinecarboxamide,
N-[2-Methyl-5-(9-oxa-3,7-diazabicyclo[3.3.1]non-3-ylcarbonyl)phenyl]-tricyclo[3.3.1.1^{3,7}]decane-1-acetamide,
or a pharmaceutically acceptable salt or solvate of any one thereof.

8. (Currently amended) ~~A composition~~ The method according to ~~any one of claims 1 to 7~~ claim 1, wherein the second active ingredient is a receptor molecule capable of binding to TNF α .

9. (Currently amended) ~~A composition~~ The method according to claim 8 wherein the second active ingredient is Etanercept.
10. (Currently amended) ~~A composition~~ The method according to ~~any one of claims 1 to 7~~claim 1, wherein the second active ingredient is an anti-TNF α antibody.
11. (Currently amended) ~~A composition~~ The method according to claim 10, wherein the second active ingredient is selected from Infliximab and Adalimumab (D2E7).
12. (Original) A kit comprising a preparation of a first active ingredient which is a P2X₇ receptor antagonist which P2X₇ receptor antagonist is an adamantyl derivative, a preparation of a second active ingredient which is a tumour necrosis factor α (TNF α) inhibitor, and instructions for the simultaneous, sequential or separate administration of the preparations to a patient in need thereof.
13. (Original) A kit according to claim 12 wherein the P2X₇ receptor antagonist is:
2-Chloro-5-[[2-(2-hydroxy-ethylamino)-ethylamino]-methyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
2-Chloro-5-[3-[(3-hydroxypropyl)amino]propyl]-N-(tricyclo[3.3.1.1]dec-1-ylmethyl)-benzamide,
(R)-2-Chloro-5-[3-[(2-hydroxy-1-methylethyl)amino]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
2-Chloro-5-[[2-[(2-hydroxyethyl)amino]ethoxy]methyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,
2-Chloro-5-[3-[3-(methylamino)propoxy]propyl]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)benzamide,
2-Chloro-5-[3-(3-hydroxy-propylamino)-propoxy]-N-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,

2-Chloro-5-[2-(3-hydroxypropylamino)ethylamino]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,

2-Chloro-5-[2-(3-hydroxypropylsulfonyl)ethoxy]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,

2-Chloro-5-[2-[2-[(2-hydroxyethyl)amino]ethoxy]ethoxy]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,

2-Chloro-5-[[2-[[2-(1-methyl-1*H*-imidazol-4-yl)ethyl]amino]ethyl]amino]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,

2-Chloro-5-piperazin-1-ylmethyl-*N*-(tricyclo[3.3.1.1]dec-1-ylmethyl)-benzamide,

2-Chloro-5-(4-piperidinyl)oxy)-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,

2-Chloro-5-(2,5-diazabicyclo[2.2.1]hept-2-ylmethyl)-*N*-(tricyclo[3.3.1.1]dec-1-ylmethyl)-benzamide,

2-Chloro-5-(piperidin-4-ylsulfinyl)-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-benzamide,

5-Chloro-2-[3-[(3-hydroxypropyl)amino]propyl]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-4-pyridinecarboxamide,

2-Chloro-5-[3-[(1*R*)-2-hydroxy-1-methylethyl]amino]propyl]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-3-pyridinecarboxamide,

5-Chloro-2-[3-(ethylamino)propyl]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-4-pyridinecarboxamide,

5-Chloro-2-[3-[(2-hydroxyethyl)amino]propyl]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-4-pyridinecarboxamide,

5-Chloro-2-[3-[(2*S*)-2-hydroxypropyl]amino]propyl]-*N*-(tricyclo[3.3.1.1^{3,7}]dec-1-ylmethyl)-4-pyridinecarboxamide,

N-[2-Methyl-5-(9-oxa-3,7-diazabicyclo[3.3.1]non-3-ylcarbonyl)phenyl]-tricyclo[3.3.1.1^{3,7}]decane-1-acetamide,

or a pharmaceutically acceptable salt or solvate of any one thereof.

14. (Currently amended) A kit according to ~~any one of claims 12 to 13~~ claim 12, wherein the second active ingredient is a receptor molecule capable of binding to TNF α .

15. (Original) A kit according to claim 14 wherein the second active ingredient is Etanercept.

16. (Currently amended) A kit according to ~~any one of claims 12 to 13~~ claim 12, wherein the second active ingredient is an anti-TNF α antibody.

17. (Original) A kit according to claim 16, wherein the second active ingredient is selected from Infliximab and Adalimumab (D2E7).

18-19. (Cancelled)

20. (Original) A method of treating an inflammatory disorder which comprises simultaneously, sequentially or separately administering:

(a) a (therapeutically effective) dose of a first active ingredient which is a P2X₇ receptor antagonist which P2X₇ receptor antagonist is an adamantyl derivative; and

(b) a (therapeutically effective) dose of a second active ingredient which is a tumour necrosis factor α (TNF α) inhibitor,
to a patient in need thereof.

21. (Original) A method according to claim 20, wherein the inflammatory disorder is rheumatoid arthritis.

22. (New) The method of claim 1, wherein the patient is treated for an inflammatory disorder.

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23. (New) The method of claim 22, wherein the inflammatory disorder is rheumatoid arthritis.